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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Mehta *et al.*		
SERIAL NUMBER:	09/351,617	EXAMINER:	P. Ponnaluri
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FOR:	GENERAL SCREENING METHOD FOR LIGAND-PROTEIN INTERACTION		

BY FACSIMILE
Commissioner for Patents
Washington, D.C. 20231

INFORMAL COMMUNICATION

In response to the Final Office Action dated November 25, 2002 ("Office Action") and in preparation for a scheduled telephonic interview with the Examiner, Applicants submit the following proposed amendments to the pending claims for consideration by the Examiner. Applicants also transmit herewith copies of Figures 2 and 3 as originally filed to aid in the Examiner's understanding of the Applicants' position.

AMENDMENTS

Claims 1, 31 and 35 have been amended as follows:

1. (Thrice amended) A method for identifying a cellular component to which a small molecule is capable of binding, comprising:

(a) providing a hybrid ligand consisting essentially of two ligands, identified as ligand A and ligand B that are linked together, wherein

(i) ligand A has a specificity for a predetermined target;

(ii) ligand A forms an irreversible covalent bond with the predetermined target;

(iii) and ligand B is the small molecule;

(b) introducing the hybrid ligand into at least one sample, the sample containing an environment, the environment containing;

(i) a first expression vector, comprising DNA encoding the target for ligand A, linked to a coding sequence for a first transcriptional module for expression as a first hybrid protein;

(ii) a second expression vector comprising a random DNA fragment encoding a polypeptide linked to a second transcriptional module for expression as a second hybrid protein; and

(iii) a third vector comprising a reporter gene wherein the expression of the reporter gene is conditioned on the proximity of the first and second hybrid proteins;

(c) permitting the hybrid ligand to bind irreversibly covalently the first hybrid protein through ligand A and the second hybrid protein through ligand B so as to activate the expression of the reporter gene;

(d) identifying those samples expressing the reporter gene; and

(e) characterizing the second hybrid protein in the samples identified in (d) so as to determine the cellular component to which the small molecule has a binding affinity.

31. (Twice amended) A kit for detecting interactions between small molecules and proteins comprising;

(a) a preactivated ligand A and reagents for forming a hybrid ligand with at least one type of ligand B, wherein ligand A has a specificity for a predetermined target and forms an irreversible covalent bond with the predetermined target;

(b) a first expression vector comprising DNA encoding a target for ligand A linked to a coding sequence for a first transcriptional module for expression as a first hybrid protein;

(c) a second expression vector comprising a random DNA fragment encoding a polypeptide linked to a coding sequence for a second transcriptional module for expression as a second hybrid protein;

(d) a third vector comprising a reporter gene wherein transcription of the reporter gene is conditioned on the proximity of the first and second hybrid proteins;

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(e) an environment for transcription and translation of the first and second hybrid proteins and reporter genes; and

(f) a means for detecting the expression of the reporter gene following the formation of a trimeric complex between the hybrid ligand and the first and second hybrid proteins.

35. (Twice Amended) A method for identifying a cellular component to which a small molecule is capable of binding, comprising:

(a) providing a hybrid ligand consisting essentially of two ligands, identified as ligand A and ligand B that are linked together, wherein

(i) ligand A has a specificity for a predetermined target;

(ii) ligand A forms an irreversible covalent bond with the predetermined target;

(iii) and ligand B is the small molecule;

(b) introducing the hybrid ligand into at least one sample, the sample containing an environment, the environment containing;

(i) a first expression vector, comprising DNA encoding the target for ligand A, linked to a coding sequence for a first transcriptional module for expression as a first hybrid protein;

(ii) a second expression vector comprising a random DNA fragment encoding a polypeptide linked to a second transcriptional module for expression as a second hybrid protein; and

(iii) a third vector comprising a reporter gene wherein the expression of the reporter gene is conditioned on the proximity of the first and second hybrid proteins;

(c) permitting the hybrid ligand to bind irreversibly covalently the first hybrid protein through ligand A and the second hybrid protein through ligand B so as to activate the expression of the reporter gene, thereby reducing a three-hybrid system to a two-hybrid system;

(d) identifying those samples expressing the reporter gene; and

(e) characterizing the second hybrid protein in the samples identified in (d) so as to determine the cellular component to which the small molecule has a binding affinity.